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Assessment of a portable clinical blood analyzer during space flight

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This study was designed to validate the utility of a commercial portable clinical blood analyzer (PCBA) in ground-based studies and on the space shuttle. Ionized calcium, pH, electrolytes, glucose, and hematocrit were determined. Results agreed well with those from traditional laboratory methods, and the PCBA demonstrated good between-day precision for all analytes. In-flight analysis of control samples revealed differences in one analyte (sodium). There were few changes in crew members' results during flight, and these were expected. Potassium increased in flight compared with before flight, and potassium, pH, and hematocrit decreased after flight. Ionized calcium was decreased in flight and on landing day. Changes during flight were likely related to sample collection technique. Postflight changes likely reflected the fluid redistribution that occurs after exposure to weightlessness. These data confirm that the PCBA is a reliable instrument for most analytes, and can provide important medical data in remote locations, such as orbiting spacecraft.

INDEXING TERMS: point-of-care testing • electrolytes • ionized calcium • pH • biosensors

Nontraditional methods are required to analyze blood samples collected in remote locations and at point-of-care testing sites. Space flight presents an unique example of a remote location where full clinical laboratory facilities are not available. Not only does the microgravity environment profoundly affect the regulatory *[1]*, musculoskeletal *[2]*, and erythropoietic *[3]* systems of the astronauts, but it also affects collection techniques and equipment that are designed to function in unit gravity. Research on human adaptation to weightlessness often involves collecting biological samples (e.g., blood, urine), which are typically stored during flight and analyzed on return to Earth. This process presents several problems, including the inability to analyze and interpret data during the mission, the need for power-consuming freezers, and the potential instability of samples during storage.

Real-time analysis of electrolytes, pH, and ionized calcium would provide valuable information for physicians responsible for providing healthcare to astronauts or other remote populations. Commercial analyzers have been developed to conduct real-time clinical chemistry analyses. The purpose of this study was to determine performance characteristics of one such portable clinical blood analyzer (PCBA), manufactured by i-STAT™, on the ground and during space flight.[4] Ground-based studies included comparison of the PCBA with standard laboratory methods. In addition, comparisons of data (aqueous controls and subject samples) were conducted before, during, and after space flight. Sodium, potassium, glucose, ionized calcium, pH, and hematocrit were analyzed with the i-STAT EC6$^+$ cartridge. For ground-based studies, venous samples were analyzed by using both the PCBA and standard laboratory methods. Capillary (fingerstick) samples are more practical for space flight applications (e.g., reduced need for phlebotomy training), and these were analyzed on the PCBA for all analytes and on the ICA2 for ionized calcium and pH determinations. For the flight studies, the PCBA was flown on five space shuttle missions, with capillary blood samples and aqueous controls being analyzed. Although no direct comparisons with other methods were available, the flight data were compared with data obtained before and after flight.

Materials and Methods

This evaluation was conducted in accordance with NCCLS and manufacturer guidelines. Several phases were

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[4] Nonstandard abbreviations: PCBA, portable clinical blood analyzer; E_A, allowable error; TE, total error; and TL_E, test limit.

Table 1. Precision statistics for the PCBA.

Analyte	Correlation (r^2)		Mean ± SD[a]	Precision estimates (SD)[b]		Total precision (SD)[b]	
				Within-run	Day-to-day	Reported[c]	Measured
Sodium	0.9996	Level 1	102.3 ± 0.2	0.4	0.0	0.61	0.44
		Level 2	140.8 ± 0.2	0.3	0.0		
		Level 3	160.8 ± 0.2	0.5	0.0	0.71	0.49
Potassium	0.9999	Level 1	2.41 ± 0.01	0.02	0.00	0.064	0.022
		Level 2	4.52 ± 0.02	0.03	0.00		
		Level 3	6.36 ± 0.03	0.04	0.01	0.047	0.048
Glucose	0.9993	Low	3.02 ± 0.03	0.05	0.02	0.08	0.05
		Medium	7.21 ± 0.03	0.06	0.00		
		High	17.66 ± 0.14	0.16	0.17	0.37	0.24
pH	0.9994	Level 1	7.166 ± 0.005	0.009	0.005	0.012	0.008
		Level 2	7.412 ± 0.002	0.005	0.001		
		Level 3	7.605 ± 0.005	0.005	0.003	0.008	0.007
Ionized calcium	0.9999	Level 1	1.558 ± 0.008	0.010	0.008	0.018	0.011
		Level 2	1.225 ± 0.008	0.015	0.005		
		Level 3	0.779 ± 0.003	0.009	0.000	0.012	0.008
Hematocrit	0.9999	Low	0.299 ± 0.002	0.002	0.002	0.007	0.003
		Medium	0.434 ± 0.004	0.005	0.003		
		High	0.467 ± 0.004	0.002	0.003	0.010	0.005

[a] Data are means ± SD of daily means; all units (except pH and hematocrit) are mmol/L.
[b] Calculated per NCCLS *[4]*.
[c] Manufacturer claims.

required to collect valid data, including instrument familiarization, calibration verification, determination of precision characteristics, method comparisons, and statistical analysis. Two studies were conducted. The first was a ground-based validation study, the second a flight study in which control and subject samples were analyzed before, during, and after flight.

SUBJECTS

For the ground-based study, 30 blood samples were drawn from 24 healthy test subjects (i.e., some subjects were tested more than once on different days). Fifteen of the subjects were men (height 178 ± 6 cm, weight 80.5 ± 9.8 kg, age 37 ± 5 years, mean ± SD) and nine were women (168 ± 7 cm, 69.6 ± 12.0 kg, 38 ± 6 years).

For the flight studies, subjects were 21 astronauts on five space shuttle missions. Eighteen of the subjects were men (height 181 ± 7 cm, weight 80.3 ± 7.3 kg, age 42 ± 6 years) and three were women (169 ± 5 cm, 65.0 ± 7.0 kg, 42 ± 4 years).

All procedures were reviewed by the Johnson Space Center Institutional Review Board to ensure ethical use of human subjects. Informed consent was obtained from all subjects.

EQUIPMENT

The PCBA (i-STAT Corp., Princeton, NJ), a hand-held, battery-powered instrument, was tested with the $EC6^+$ cartridge. Electrolytes are determined through ion-selective electrode potentiometry, glucose through amperometry, hematocrit through conductometrics, and pH through direct potentiometry. Hemoglobin is calculated from the hematocrit (hemoglobin = hematocrit × 34), and is not directly measured. Approximately 85 μL of whole blood are required for this panel.

For the ground-based study, PCBA results were compared with traditional laboratory methods: ionized calcium and pH, ICA2 Ionized Calcium Analyzer (Radiometer, Copenhagen, Denmark); sodium, potassium, and glucose, CX5 Chemistry Analyzer (Beckman Instruments, Brea, CA); hematocrit, microcapillary centrifuge (Miles Laboratories, Elkhart, IN). All analyses were conducted at the Johnson Space Center Clinical Laboratory. This laboratory is accredited by the College of American Pathologists.

SAMPLE COLLECTION AND PROCESSING

Ground-based study. Capillary samples were collected from each subject by fingerstick with a lancing device and balanced heparin capillary tubes (Radiometer). Blood was mixed with a mixing wire ~20 times before being analyzed with the PCBA and ICA2 for ionized calcium and pH. This procedure is recommended for the ICA2, and was used only for the ground-based study to allow for consistency between methods. Each sample was analyzed within 3 min of collection. Immediately after the fingerstick, whole blood was collected by venipuncture (one lithium heparin sample and one tripotassium EDTA sample). The lithium heparin specimen was analyzed with the PCBA and ICA2 for ionized calcium and pH within 10 min of collection. After centrifugation of the lithium heparin sample, plasma was analyzed for sodium, potas-

Table 2. Method comparison statistics.

	PCBA capillary	PCBA venous	Reference venous	TE[a] Capillary–Venous	TE[a] Venous–Venous	E_A[b]	PCBA control	Reference control
Sodium, mmol/L	141.4 ± 1.3[f]	139.6 ± 1.4	139.3 ± 1.4[c]	2.1	0.3	4.0	140.5 ± 17.0[h]	148.4 ± 17.8[c]
Potassium, mmol/L	4.27 ± 0.37[f]	4.10 ± 0.24[g]	4.13 ± 0.26[c]	0.14	0.02	0.5	4.41 ± 1.64[h]	4.80 ± 1.74[c]
Glucose, mmol/L	5.42 ± 1.14	5.42 ± 1.12	5.46 ± 1.29[c]	0.04	0.05	0.33	9.30 ± 6.27[h]	8.56 ± 5.96[c]
Ionized calcium, mmol/L	1.226 ± 0.044[f]	1.183 ± 0.033[g]	1.197 ± 0.043[d]	0.049	0.034	—	1.197 ± 0.331	1.118 ± 0.320[d]
pH	7.397 ± 0.026	7.376 ± 0.030[g]	7.388 ± 0.031[d]	0.013	0.016	0.04	7.391 ± 0.180[h]	7.406 ± 0.189[d]
Hematocrit	0.428 ± 0.034[f]	0.427 ± 0.033	0.419 ± 0.035[e]	0.021	0.019	—	0.396 ± 0.072[h]	0.342 ± 0.105[e]

[a] TE = total error calculated as described in text.
[b] E_A = allowable error (from ref. 6).
[c] Reference sample analyzed using CX5.
[d] Reference sample analyzed using ICA2.
[e] Reference sample analyzed using microcentrifuge.
[f] Significant ($P < 0.05$) difference between capillary blood analyzed with PCBA and venous blood analyzed with reference method.
[g] Significant ($P < 0.05$) difference between venous blood analyzed with PCBA and venous blood analyzed with reference method.
[h] Significant ($P < 0.05$) difference between control sample analyzed with PCBA and control sample analyzed with reference method.

sium, and glucose with the CX5. The EDTA whole-blood specimen was analyzed with the microcentrifuge for hematocrit. Each capillary sample was assayed singly; venous samples were run in duplicate.

Flight study. Crew members collected capillary samples from each other by fingerstick with a lancing device and balanced heparin capillary tubes (Radiometer). Blood was quickly transferred to the cartridge for PCBA analysis. Samples obtained before and after flight were collected either by crew members or by medical technologists. Blood samples were scheduled to be collected three times before flight, twice during flight, and three times after flight [landing day = return + 0 days (R + 0), and on R + 3 and R + 6 days]. Control samples (two levels; Bionostics Corp., Actin, MA) were run every day that blood samples were collected.

ASSESSMENT OF IMPRECISION AND LINEARITY (GROUND-BASED STUDY)

Verification of instrument calibration throughout the reportable range for each analyte (except hematocrit) was determined by analysis of five assayed solutions (i-STAT Corp.). Linearity was determined by using regression analysis. Analytical imprecision (within-run and between-day) was estimated according to NCCLS guidelines *[4]* from the analysis of three controls (i-STAT Corp.). Measurements were performed twice at the beginning and twice at the end of each run for 5 days. Verification for hematocrit was assessed by using lithium heparin-anticoagulated blood samples (n = 3). Each of these samples was analyzed four times with the PCBA and the microcentrifuge, and results were compared. Precision (within-run and between-day) was estimated for hematocrit by using three levels of Meter Trax controls (Hematronix, Benicia, CA). Total precision was determined for each analyte with two controls representing high and low medical decision levels *[5]*, and compared with manufacturer claims per NCCLS guidelines *[4]*.

STATISTICAL ANALYSES

Ground-based study. Comparisons between our results and the performance data supplied by the manufacturer were made by using the χ^2 test as per NCCLS *[4]*. This test compares the estimate of total precision with that claimed by the manufacturer and determines whether measured estimates are statistically higher.

Linear regression analyses of the analytical methods were performed for all analytes; comparison plots of the PCBA data vs the reference method were prepared. The range of clinical data was considered adequate if the correlation coefficient equaled or exceeded 0.975 *[5–8]*. When the range was adequate, data dispersion around each regression line was estimated by calculating the standard error of the estimate ($S_{y|x}$), and both proportional (slope) and constant (intercept) error were evaluated. Systematic, random, and a point estimate of the total error (systematic plus random

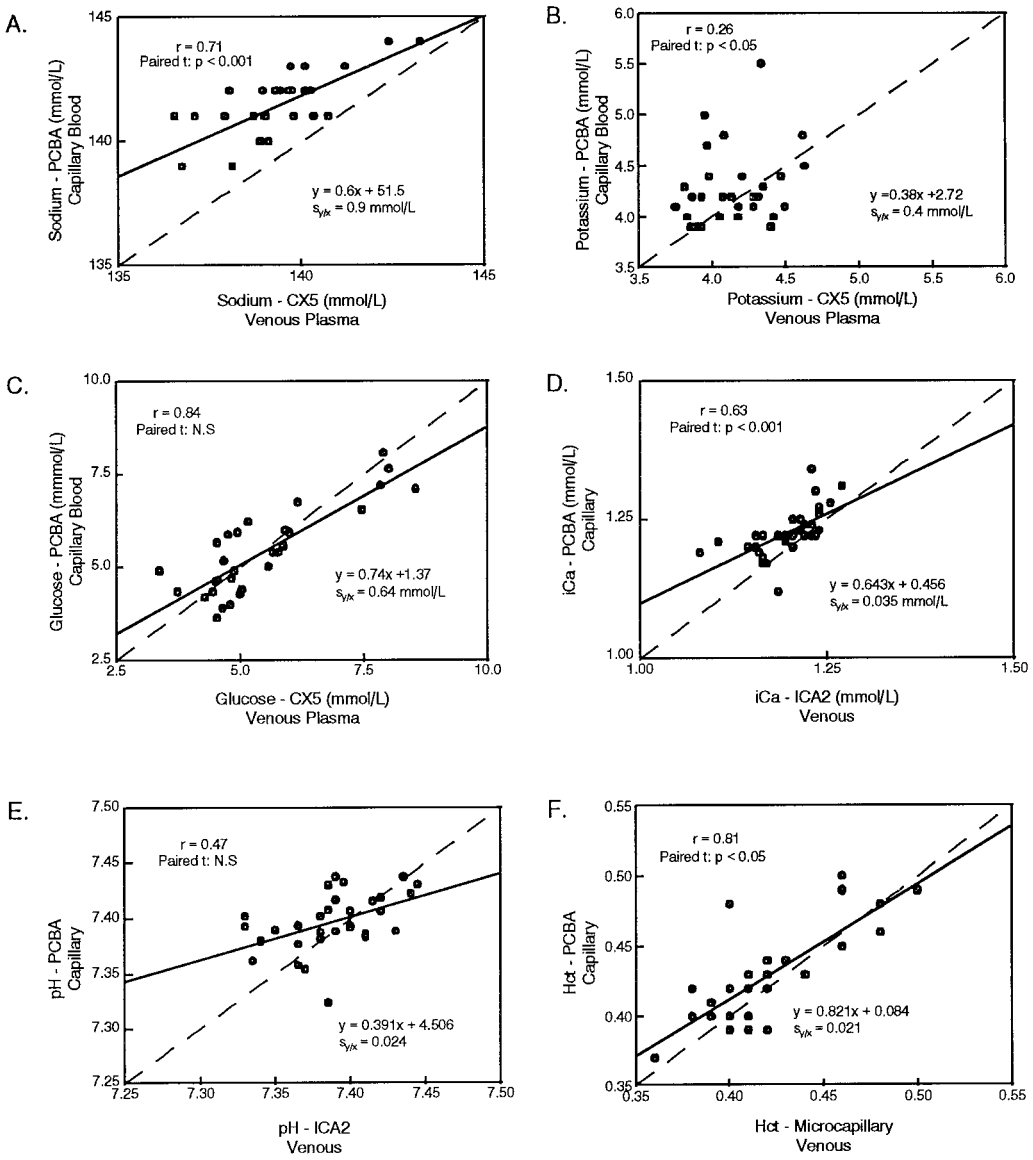

Fig. 1. Comparison plots of paired capillary blood samples analyzed with the PCBA and venous blood samples analyzed with comparison methods for (*A*) sodium, (*B*) potassium, (*C*) glucose, (*D*) ionized calcium, (*E*) pH, and (*F*) hematocrit.

Dotted lines represent the line of identity; *solid line* represents the results of linear regression analysis.

errors) were calculated when the range was adequate *[6, 8, 9]*. In these cases, clinical significance was evaluated by comparing the total error estimate provided by the regression data at the medical decision level for each analyte *[6, 8, 9]* with the allowable error (E_A) as defined by CLIA (1988) *[6]*. When the range was not adequate, total error (TE) was estimated as: TE = 4 SD + bias *[6]*, where SD is the between-day SD for the level 2 control (which was in a range similar to the subject data). The TE was compared with CLIA definitions. For all analytes, outliers were determined after calculation of the test limit (TL_E) and relative TL_E *[7]*. Data points that failed both tests were defined as outliers, and the results reevaluated after elimination of the suspect data. Data in the Tables describe the raw data without removal of outliers.

Bias plot analysis was used to compare the PCBA data with the comparison method for each analyte. Paired two-tailed *t*-tests *[5, 10]* were used to assess the difference between the PCBA and the reference method for each analyte. CLIA's E_A *[5]* were available for all analytes except for ionized calcium and hematocrit. The PCBA determination was considered acceptable if the TE (determined from the regression line or calculated as described above) was within CLIA's E_A *[6]*.

The PCBA was also evaluated over a wider analytical range than provided by the subjects. Linear regression analysis, bias plot analysis, and paired *t*-tests were used to compare data obtained from aqueous control samples analyzed with the PCBA and the comparison method for all analytes. Acceptable errors were not compared for

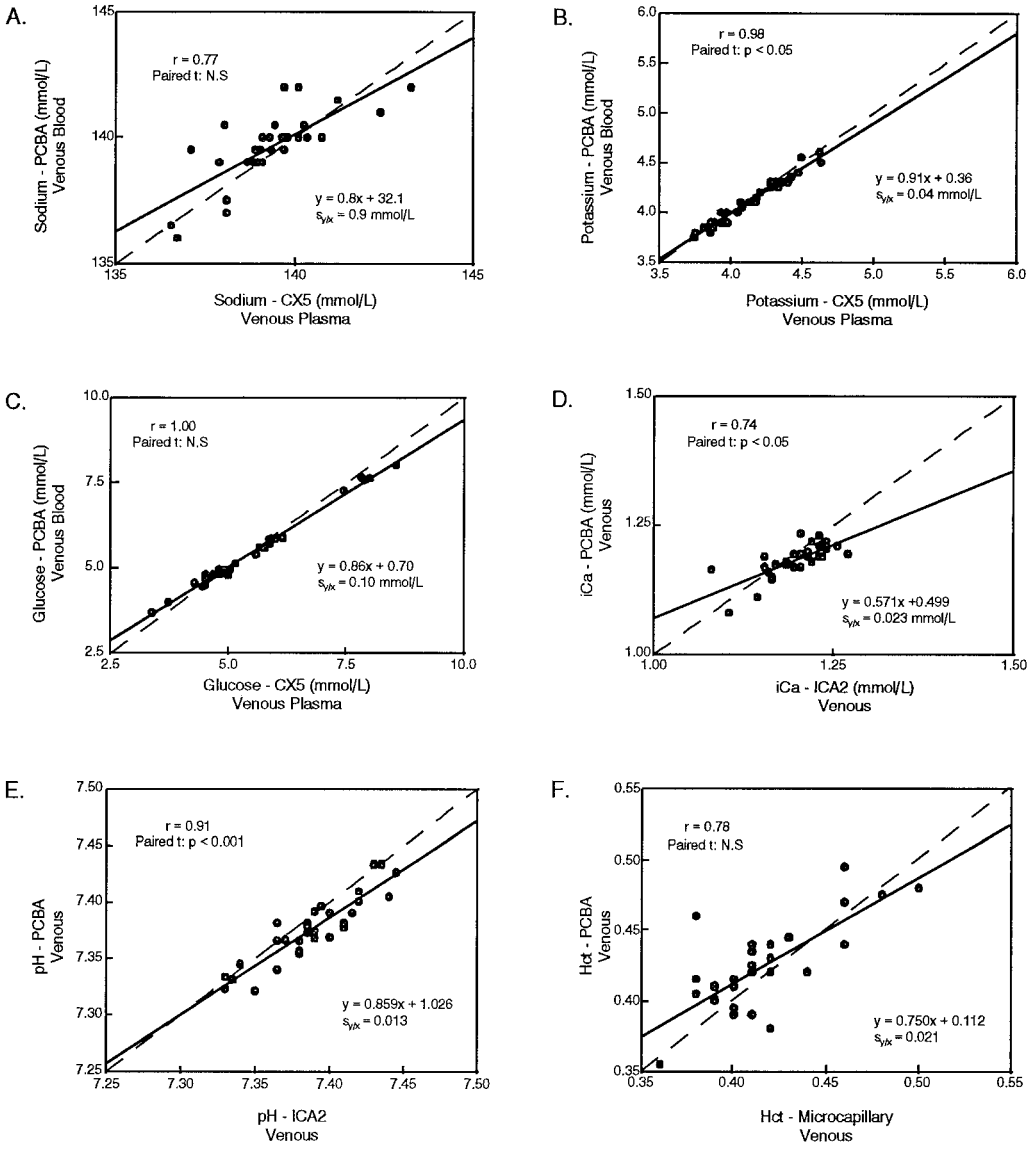

Fig. 2. Comparison plots of paired venous blood samples analyzed with the PCBA and venous blood samples analyzed with comparison methods for (*A*) sodium, (*B*) potassium, (*C*) glucose, (*D*) ionized calcium, (*E*) pH, and (*F*) hematocrit.
Dotted lines represent the line of identity; *solid line* represents the results of linear regression analysis.

these aqueous controls because they are repeated analyses of three samples (three levels of controls). Mean values represent averages of all analyses.

Flight study. Data were analyzed in their raw form or were transformed for normality as defined by the Kolmogorov–Smirnov normality test with Lilliefors' correction *[11]*. The reciprocal of glucose (control and subject data) and potassium (subject data) values were successful in normalizing the data and were used for statistical analysis. All other analyses were performed on the raw data. The repeated-measures ANOVA model with a priori contrasts (i.e., contrasts planned before data analysis was undertaken) was used to investigate differences between ground and flight values (control samples) and data obtained before, during, and after exposure to microgravity (subject data).

Only control data where identical lot numbers were used on the ground and in flight within mission were analyzed. The resulting data set consisted of 10 samples (5 of each level of i-STAT control) measured over time: four times on the ground and twice in flight. No control samples were analyzed for hematocrit. Comparisons were made between the means of four ground-based data points and the means of two flight values.

Data were missing on one flight day from five subjects. To maximize sample size, the in-flight data were averaged, and a priori contrasts were used to compare data obtained before, during (average in flight), and after flight

Table 3. Capillary determinations of ionized calcium and pH with the PCBA and ICA2.

	PCBA capillary	Reference capillary	TE[a]	E_A[b]
Ionized calcium, mmol/L	1.226 ± 0.044	1.235 ± 0.035[c]	0.029	—
pH	7.397 ± 0.026[d]	7.425 ± 0.019[c]	0.032	0.04

[a] TE = total error calculated as described in text.
[b] E_A = allowable error (from ref. *6*).
[c] Reference sample analyzed using ICA2.
[d] Significant ($P < 0.05$) difference between capillary blood analyzed with PCBA and capillary blood analyzed with reference method.

(3 postflight days). Planned comparisons were made between the mean of three preflight data points, the in-flight average, and each of three postflight data points. Data were analyzed with Super Anova (Abacus Concepts, Berkeley, CA) and Sigma Stat (Jandel Scientific Software, San Rafael, CA). The precision of the experiment design to detect differences between PCBA performance on the ground and during space flight was evaluated. Since the ANOVA tests the null hypothesis that there are no mean differences between data collected in flight and on the ground, the determination of a lack of significant difference in those means does not imply that there are no differences. Rather, it implies that any differences were too small to be detected with the design used. Estimates of the detectable effect were obtained for values of $\alpha = 0.05$, power = 0.95, and the estimate of the variance for the effect from the ANOVA for the control data. These calculations determine the minimum difference required for statistical significance. Thus, if significant differences are not found, differences between flight and ground data are likely to be less than those obtained.

Results

GROUND-BASED STUDY

Calibration throughout the reportable ranges of the PCBA was verified for all analytes (Table 1). Evaluation of total precision by χ^2 analysis showed excellent agreement with the manufacturer claims for all analytes.

Sodium values from capillary blood analyzed with the PCBA were higher ($P < 0.05$) than those from venous plasma analyzed with the CX5 (Table 2). Venous samples did not differ between methods. No outliers were identified, and the calculated TE for both comparisons were well within CLIA's E_A of 4.0 mmol/L *[6]*. Control concentrations of sodium were lower when measured by the PCBA than by the CX5.

Poor correlation was observed (Fig. 1) between PCBA potassium values from capillary samples compared with venous plasma samples analyzed with the CX5. No outliers were identified, and the calculated TE was within CLIA's E_A of 0.5 mmol/L (Table 2). Potassium values from venous blood samples (PCBA) were better correlated and less variable than capillary blood samples when compared with venous plasma samples on the CX5 (Fig. 2). Because the range was adequate, estimates of random error and total systematic error were calculated *[6, 8]*. Random error was 0.07 mmol/L; the systematic error calculated at medical decision levels of 3.0 and 6.0 mmol/L was +0.08 and −0.19 mmol/L. Thus, the total error from the regression data was 0.15 and 0.26 mmol/L at medical decision levels of 3.0 and 6.0 mmol/L, respectively (all within the E_A of 0.5 mmol/L *[6]*). The calculated TE was also within CLIA's E_A. The variability of the control-solution values around the regression line was minimal ($S_{y|x} = 0.09$ mmol/L). PCBA potassium concentrations were lower in controls ($P < 0.001$) and venous samples ($P < 0.05$) and were higher in capillary samples ($P < 0.05$) when compared with determinations on the CX5.

PCBA glucose values obtained from capillary samples correlated well when compared with CX5 analysis of venous samples (Fig. 1); however, correlation was markedly improved in comparisons of PCBA venous blood samples with CX5 venous plasma samples (Fig. 2). Random error was 0.22 mmol/L; the systematic error calculated at medical decision levels of 2.78 and 6.66 mmol/L

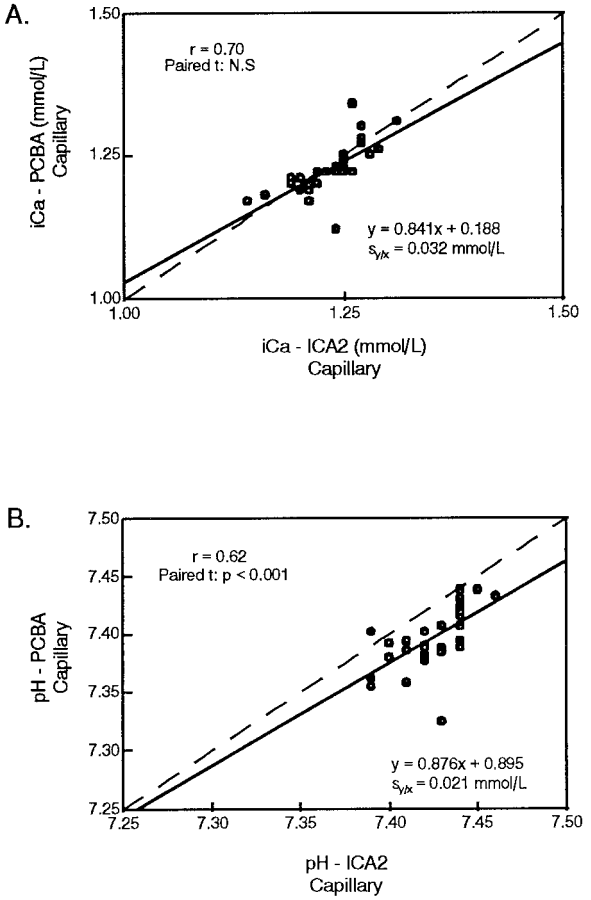

Fig. 3. Comparison plots of paired capillary blood samples analyzed with the PCBA and capillary blood samples analyzed with comparison methods for (*A*) ionized calcium and (*B*) pH.

Dotted lines represent the line of identity; *solid line* represents the results of linear regression analysis.

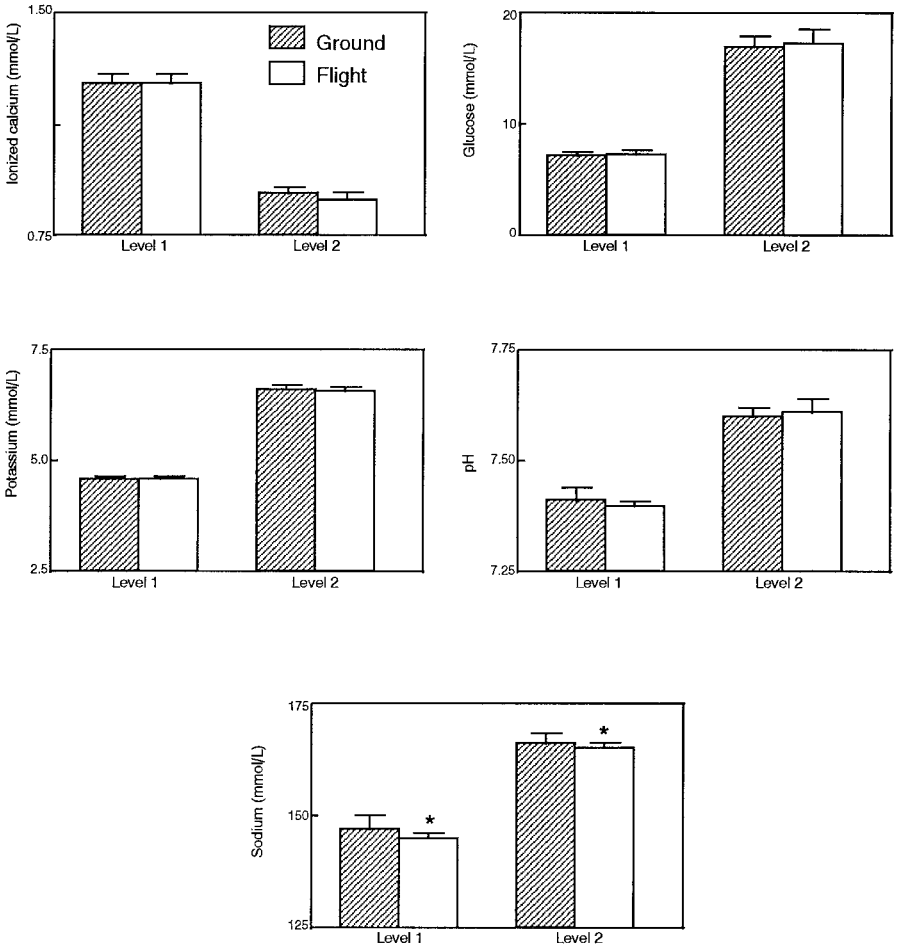

Fig. 4. Flight control data.

*, significant ($P < 0.05$) difference between ground and flight analyses.

were +0.33 and −0.22 mmol/L. The total errors from the regression data were 0.55 and 0.44 mmol/L, compared with CLIA's E_A of 0.33 and 0.66 mmol/L *[6]*, respectively. However, all glucose determinations by the PCBA were similar to those on the CX5, and the calculated TEs were within CLIA's E_A. Control samples were increased on the PCBA compared with the CX5 ($P < 0.001$). No outliers were identified for any of the glucose analyses.

Ionized calcium in venous blood samples measured with the PCBA demonstrated slightly improved correlation and reduced variability (vs capillary samples) relative to venous blood samples analyzed with the ICA2 (Fig. 2). Control data correlated well ($r = 1.00$) and values did not differ between methods. Poor correlation was observed for pH data obtained from capillary samples analyzed with the PCBA relative to ICA2 analysis of venous samples (Fig. 1). Venous samples showed much improved correlation and were less variable (vs capillary samples) relative to the reference method (Fig. 2). The calculated TEs for both PCBA analyses were within CLIA's E_A (0.04 *[6]*). Control data correlated well ($r = 1.00$), and were higher on the PCBA than on the ICA2 ($P < 0.05$). ICA2 determination of ionized calcium and pH of venous samples were lower and higher, respectively, than capillary and venous values on the PCBA. No outliers were identified for the pH or ionized calcium analyses.

Capillary samples were analyzed with both the PCBA and the ICA2 for pH and ionized calcium (Table 3). For ionized calcium, the PCBA data correlated with those of the ICA2 (Fig. 3), and one outlier was identified from $TL_E = 0.091$ mmol/L. Elimination of the outlier had minimal impact on correlation ($r = 0.80$ vs 0.70), the calculated bias (−0.005 ± 0.025 vs −0.009 ± 0.032 mmol/L, not significant), or calculated TE (0.025 vs 0.029 mmol/L). The mean capillary pH measured with the PCBA was lower ($P < 0.001$) than the capillary reference mean (Table 3). The calculated TE (Table 3) was within CLIA's E_A *[6]*.

PCBA hematocrit values obtained from capillary samples correlated well with microcentrifuged venous samples (Fig. 1). Hematocrit measured in capillary blood with the PCBA was higher ($P < 0.05$) than that of the venous reference (Table 2). One outlier was identified from $TL_E = 0.068$. Elimination of the outlier had minimal effect on correlation ($r = 0.87$ vs 0.81) and calculated TE (0.018 vs

Table 4. Minimum detectable differences between ground and flight control data.

Analyte	Minimum detectable difference, %[a]
Glucose	0.3
Ionized calcium	2.0
Sodium	0.8
pH	0.2
Potassium	0.6

[a] Values are percent of the mean (α = 0.05, power = 0.95).

0.021). However, the calculated bias was no longer statistically significantly different (+0.006 ± 0.018 vs +0.009 ± 0.021). The use of venous blood to determine hematocrit with the PCBA did not improve the correlation of this measure (vs capillary samples) relative to hematocrit determined by the reference method (Fig. 2). No outliers were identified, and venous analyses were similar between methods. Whole-blood controls analyzed on the PCBA correlated well with microcentrifugation analyses; however, values on the PCBA were higher (P <0.001, Table 2).

FLIGHT STUDY

The astronauts reported that the analyzer functioned well during space flight, and the data support this information. Analysis of both levels of controls were similar on the ground compared with flight for all analytes except sodium (Fig. 4). In-flight sodium analyses were lower (P <0.05) than ground-based determinations (Level 1: 145 ± 1 vs 147 ± 3; Level 2: 165 ± 1 vs 166 ± 1); however, the differences were within CLIA's performance limits and likely do not reflect analytical problems in microgravity. The detectable differences (expressed as percentage of the mean) for the control data are shown in Table 4. These differences are sufficiently small (2% or less) for all analytes not found significantly different. This indicates that the information provided by the PCBA in microgravity for those analytes is probably little different from that obtained on the ground. For analytes for which significant differences were found, differences in Table 4 also indicate why such small magnitudes of differences could be detected and why they are of little practical importance.

The only measured changes in the subject data during space flight (compared with before flight) were a slight (but statistically significant) increase in blood potassium (Fig. 5), and a slight (but statistically significant) decrease in ionized calcium. Glucose results were relatively more variable (compared with other data); however, fasting was not a constraint of this experiment.

After flight, there were statistically (but not clinically) significant decreases in blood potassium, ionized calcium, and pH on R + 0 (Fig. 5) compared with preflight values. The values returned to preflight concentrations by R + 3 (pH and ionized calcium) and R + 6 (potassium). Hematocrit values were similar to preflight values on landing day, and lower on R + 3 and R + 6 (Fig. 5).

Discussion

The results from this study demonstrate the utility of the PCBA for real-time clinical chemistry analyses, both on Earth and during space flight. Since capillary blood more closely approximates arterial compared with venous blood, some variability is to be expected.

Electrolyte values in venous samples were generally similar when analyzed with the PCBA or reference methods. The capillary data (compared with venous) were less reliable, especially for potassium. This may have resulted either from contamination of capillary samples with tissue fluid possibly from use of an automated lancet, pressure applied to the finger, or from increased hemolysis caused by using a mixing wire. There were more discrepancies between PCBA and reference determinations of electrolytes in control solutions compared with the analysis of blood samples. There were slight differences in venous samples between methods, whereas capillary–venous differences were more notable. The reason for this is unclear, although matrix differences may be partially responsible. Although the calculated errors for potassium were within the E_A *[6]*, the poor correlation observed in the capillary–venous comparison plots suggests that these results should be interpreted cautiously.

Glucose values in venous or capillary samples determined with the PCBA were similar to those generated with reference techniques. Glucose concentrations are typically 0.11–0.28 mmol/L greater in capillary vs venous blood in fasting individuals *[12]*, and are even greater after a glucose load; however, these subjects were not required to be fasting. Plasma glucose generally is more stable than whole-blood glucose *[12]* because of cellular glucose utilization before analysis; however, the PCBA samples were analyzed quickly, which probably minimized this effect.

With regard to ionized calcium, both venous and capillary samples yielded satisfactory results. This is important for research at NASA, as changes in bone and calcium homeostasis are critical issues in understanding human adaptation to extended-duration spaceflight *[2]*. Heparin may interfere with ionized-calcium measurement *[13, 14]*, although our evaluation data (using balanced heparin capillary tubes) suggest that whole-blood specimens can also provide valuable results.

Analysis of pH in capillary samples (PCBA) vs venous samples (ICA2) were satisfactory as determined by CLIA *[6]*. Physiologic arterial–venous differences in pH typically range from 0.01 to 0.03 *[15]*. In this study, capillary–venous differences were 0.01 (PCBA) and 0.04 (ICA2).

Venous samples did not provide much improvement for hematocrit compared with capillary samples. Although the response for control solutions demonstrated good correlation, the bias data were not randomly distributed, with almost 50% error at the low end of the scale.

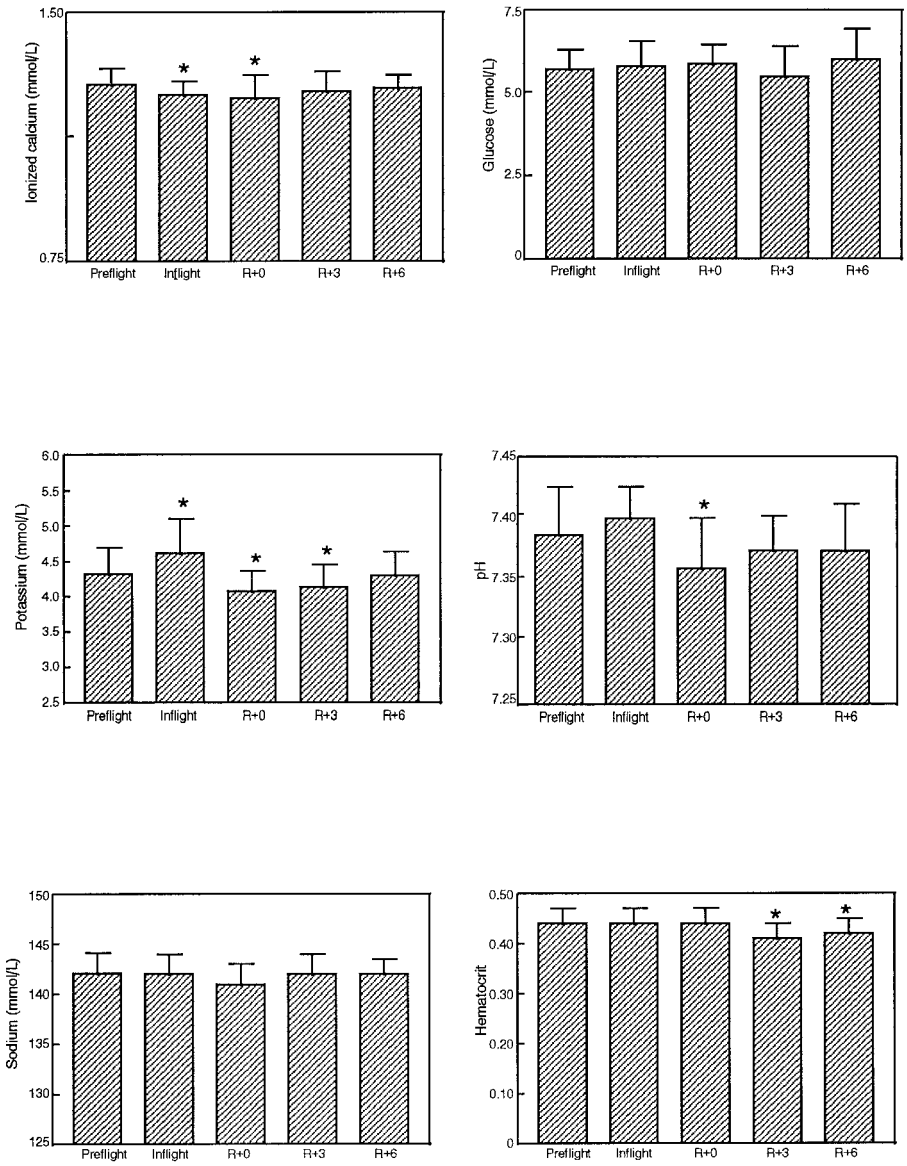

Fig. 5. Flight subject data.

*, significant ($P < 0.05$) difference between in-flight or postflight analysis when compared with preflight analysis. R + x = return + x days, where R + 0 = landing day.

Similar concerns have been expressed with regard to hematocrit determination with the i-STAT EC6$^+$ cartridge *[16, 17]*. Potential sources of error reported by the manufacturer (i-STAT Corp.) include anticoagulant effects on blood cell size (primarily with the microcapillary technique) and interference from electrolyte, protein, or lipid content of samples with conductometric techniques, such as that used by the PCBA. The determination of hematocrit, as described here, is still of concern. Moreover, as the hemoglobin data are calculated from the hematocrit, they too should be interpreted with caution.

Although comparisons of PCBA determinations with standard techniques during space flight were not available, the data presented here provide clear evidence that the PCBA functions well during space flight. The control data show good agreement between ground-based and flight analyses, and the lower sodium values observed during flight are within acceptable performance limits.

Data from shuttle crew members suggest that there is little effect of microgravity on the concentration of the circulating analytes examined in this study. The changes observed in flight and landing samples were not at amounts considered clinically significant, rapidly returned to preflight concentrations, or were related to known physiological adaptations to space flight. Increased potassium concentrations may be related to sample collection technique, in that fingerstick samples often have increased potassium concentrations. Similarly, decreases in ionized calcium in flight and on landing day may reflect sample handling. Decreases in ionized cal-

cium as a consequence of delayed analysis have been observed in ground studies. The decrease in postflight hematocrit is related to the decreased red blood cell mass that occurs after space flight *[3]* accompanied by the rapid return of plasma lost during space flight *[1]*.

In summary, capillary blood samples can be used to assess ionized calcium and pH with the PCBA. Nevertheless, in most instances, use of whole blood with the PCBA greatly improves agreement with traditional laboratory methods. The PCBA showed good precision in assessments of most analytes evaluated in this report, and performed well compared with traditional methods, with the exception of hematocrit. These data demonstrate the utility of the PCBA in a microgravity environment, and will provide important information regarding crew health during space flight.

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